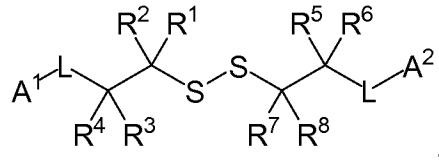


CLAIMS READABLE ON ELECTED SPECIES

- 1-6. (canceled)
7. (previously presented) A disulfide bond-containing crosslinking agent comprising:
  - a) a disulfide bond;
  - b) at least one electron withdrawing group wherein proximity of said electron withdrawing group to said disulfide bond results in said disulfide bond being cleaved more rapidly than oxidized glutathione in physiological conditions; and,
  - c) two reactive groups independently selected from the group consisting of: isothiocyanate, isocyanate, acyl azide, maleimide, urea, aldehyde, ketone, epoxide, carbonate, activated carboxylate, acryloyl derivative, primary amine, aziridine derivative, carbamate, diol, hydrozide derivative and anhydride, wherein:
    - i) one reactive group is located on each side of said disulfide bond, but not between said electron withdrawing group and said disulfide bond;
    - ii) said reactive groups are capable of forming covalent bonds with separate compounds on each side of said disulfide bond;
    - iii) formation of said covalent bonds does not result in loss of said electron withdrawing group, cleavage of said disulfide bond, or said disulfide bond not being cleaved more rapidly than oxidized glutathione; and,
    - iv) subsequent cleavage of said disulfide bond results in the formation of two molecules.

8. (previously presented) The disulfide bond-containing crosslinking agent of claim 7 wherein disulfide bond-containing crosslinking agent consists of the structure selected from the group consisting of:



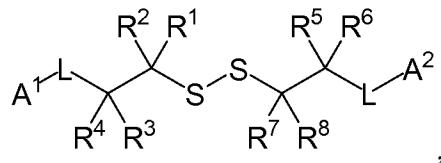
wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ , and  $\text{R}^8$  are independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aralkyl, aralkenyl, or aralkynyl, heteroatom (N, O, S), carbonyl group, and electron withdrawing group, at least one of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ , or  $\text{R}^8$  consists of an electron withdrawing group, X consists of a heteroatom selected from the group including sulfur, oxygen, nitrogen, and phosphorus, L consists of a linker group that provides a connection between the disulfide bond and the reactive groups, and  $\text{A}^1$  and  $\text{A}^2$  are reactive groups.

9-18. (canceled)

19. (previously presented) A disulfide bond-containing crosslinking agent comprising:

- a disulfide bond;
- at least one electron withdrawing group wherein proximity of said electron withdrawing group to said disulfide bond reduces the pKa of at least one of the constituent thiols of said disulfide bond to less than glutathione thiol pKa; and,
- two reactive groups independently selected from the group consisting of: isothiocyanate, isocyanate, acyl azide, maleimide, urea, aldehyde, ketone, epoxide, carbonate, activated carboxylate, acryloyl derivative, primary amine, aziridine derivative, carbamate, diol, hydrozide derivative and anhydride, wherein:
  - one reactive group is located on each side of said disulfide bond, but not between said electron withdrawing group and said disulfide bond;
  - said reactive groups are capable of forming covalent bonds with separate compounds on each side of said disulfide bond;
  - formation of said covalent bonds does not result in loss of said electron withdrawing group, cleavage of said disulfide bond, or an increase in the pKa of at least one of the constituent thiols of the disulfide bond such that said pKa is not less than glutathione thiol pKa; and,
  - subsequent cleavage of said disulfide bond results in the formation of two molecules.

20. (previously presented) The disulfide bond-containing crosslinking agent of claim 19 wherein disulfide bond-containing crosslinking agent consists of the structure selected from the group consisting of:



wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> are independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aralkyl, aralkenyl, or aralkynyl, heteroatom (N, O, S), carbonyl group, and electron withdrawing group, at least one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, or R<sup>8</sup> consists of an electron withdrawing group, X consists of a heteroatom selected from the group including sulfur, oxygen, nitrogen, and phosphorus, L consists of a linker group that provides a connection between the disulfide bond and the reactive groups, and A<sup>1</sup> and A<sup>2</sup> are reactive groups.

21-23. (canceled)

24-28. (canceled)

Remarks

Rejection of the claims under 35 USC §102:

Claims 7, 8, 19, and 20 have been rejected under 35 U.S.C. 102(b) as being anticipated by Abderhalden et al. (Berichte der Deutschen Chemischen Gessellschaft 1916). The action states that the compound taught by Abderhalden et al. anticipates Applicants' claims. Applicants respectfully disagree. Applicants' claim requires that the compound have "at least one electron withdrawing group wherein proximity of said electron withdrawing group to said disulfide bond results in said disulfide bond being cleaved more rapidly than oxidized glutathione in physiological conditions" or "reduces the pKa of at least one of the constituent thiols of said disulfide bond to less than glutathione thiol pKa" (step b). In Applicants' prior amendment, Applicants noted that the structure disclosed by Abderhalden et al. contains a primary amine group. However, as noted in Applicants amendment of Aug 13, 2008, the structure disclosed by Abderhalden does not contain "at least one electron withdrawing group wherein proximity of said electron withdrawing group to said disulfide bond results in said disulfide bond being cleaved more rapidly than oxidized glutathione in physiological conditions". In support of this argument, Applicants have again provided, with this amendment, the previously submitted declaration under 37 C.F.R. 1.132 showing that the Abderhalden et al. compound does not contain a disulfide bond that is cleaved more rapidly than oxidized glutathione or have a pKa of at least one of the constituent thiols that is less than glutathione thiol pKa.

The Examiner's rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 7, 8, 19, and 20 should be allowable.

Respectfully submitted,

/Kirk Ekena/  
Kirk Ekena, Reg. No. 56,672  
Roche Madison Inc.  
505 South Rosa Road  
Madison, WI 53719  
608-238-4400

I hereby certify that this correspondence is being transmitted to the USPTO on this date: 11/20/2008.

/Kirk Ekena/  
Kirk Ekena